January 16, 1956

Dear Gene:

Having had a chance to look through your very valuable review, I jotted down a few comments for my own benefit, but thought you might be interested to read them. Any criticisms must be measured against my unstinting admiration for the whole job.

1. P.15 The analogy with molecular ecology is rather fuzzy, though not much more so than the original concept.

p.19

2. I would be interested to know more precise measurements comparing activities of whole cells and extracts. In E. coli (cf. my J Bact paper) you can get a 100-fold increase of lactase activity by opening the cells; Botis Rotman has been working on this, and it's a complicated business. The same holds for many other microbial enzymes. The nearest analogy I can think of is the "activation" of the respiration of eggs by fertilization and by uncoupling agents.

3. P. 28 Do you believe Meinland's story, and the related one of blood invertase? I'm always afraid the old boys did not have sufficient respect for bacterial contamination as a source of the enzymes-- and were the methods crude! Is there much point dignifying lactase as b-galactosidase, where it has not been assayed on other glycosides? (Actually, the coli lactase should be called a b-galafuranosidase, since a-L-arabinosides are also split.

4. p.98 Gunn (Physiol. Rev., 3,) quotes a paper by Schinz, which probably implies that atropine esterase can be adaptive in rabbits. Have you seen this? I am surprised you did not quote the old classics of Hausmann and Gunn (which Otto Loewi led me to).

5. Actually, colchicine in the hands of Dustin and others (see Eigsti's book for references) was an important agent used by many European workers in the 1930's to provoke the "alarm reaction"-- the last sentence reads too casually --that is there must be much more direct evidence of cortical effects of colchicine.

6. p.117 Have you run into any other references to strain differences in drug response?

7. 99-100. Are you acquainted with Cantoni & Bernheimer's work on strep toxins and tolerance- J Pharm etc? There is another interesting paper by Goldblatt on renin which proposes a mechanism of tolerance (Am J Physiol '53).

Sincerely,

Joshua Lederberg